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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09 996,738	11 30 2001	Philip Gotwals	A076 US	4464

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John T. Li
BIOGEN, INC.
14 Cambridge Center
Cambridge, MA 02142

EXAMINER

HADDAD, MAHER M

ART UNIT	PAPER NUMBER
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1644

9

DATE MAILED: 02 11 2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/996,738

Examiner

Maher M. Haddad

Applicant(s)

GOTWALS ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5. 6) ☐ Other: ____

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DETAILED ACTION

1. Claims 1-7 are pending and currently under examination.
2. Claim 1 is objected to under 37CFR 1.821(d) for failing to recite the SEQ ID NO. in the claim.
3. There appear to be discrepancy between the paper copy of the Sequence Listing, Figure 15 and the specification. For example, the amino acid numbers of SEQ ID NO: 6 and the highlighted box of Figure 15 do not match with the amino acid residues 92-97, Val-Gln-Arg-Gly-Gly-Arg in claim 1 and page 2, lines 1-6 of the specification. It appears that Val-Gln-Arg-Gly-Gly-Arg are at amino acid positions 91-96 of SEQ ID NO: 6 and Figure 15. Clarification is required.
4. The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Figure 15, on page 6, line 12 has described the amino acid sequence of the human α 1-I domain that must have a sequence identifier. Correction is required.
5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(c) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(c) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(c)).
6. Claim 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,788,966 (IDS Ref. No. AA).

The '966 patent teaches a method for treating arthritis (see the entire document and column 10, reference claims 1-8 and column 8 lines 65-67 in particular) that is associated with elevated levels of VLA-1 comprising administering to a human a monoclonal antibody 1B3.1 or a fragment thereto (column 3 lines 5-10) that inhibits collagen binding to VLA-1 (see entire document and reference claims 1-8, column 10 in particular). Furthermore, the '966 reference teaches that 1B3.1 antibody recognizes an epitope on VLA-1 protein (see column 8 lines 39-46 in particular). The term "comprises" in claim 1 is open-ended so that the epitope may include additional amino acids on either or both of the N- or C- termini of given sequence.

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The recitation of "decrease in arthritis score of about 65%, 79%, 85%, 90% or greater" of claims 1-4 is considered inherent properties of the reference antibody because the antibody 1B3.1 used in the reference method is the same as the antibody used in claimed method.

While the prior art teachings may be silent as to the "function blocking antibody" per se: the method, the product used in the reference method are the same as the claimed method. Therefore "a function blocking antibody" is considered inherent property.

Since the office does not have a laboratory to test the reference antibody it is applicant's burden to show that the reference antibody does not bind to the epitope comprises amino acid residues and does not decrease in arthritis score of about 65%, 79%, 85%, 90% or greater recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,788,966 (IDS Ref. No. AA), in view of Riikonen *et al* (Biochemical and Biophysical Research Communication 209:205-212, 1995) and Fabbri *et al* (IDS Ref. No. CB).

The teachings of '966 patent have been discussed, *supra*. The '966 further teaches that members of a protein complex called very late antigens (VLA) are expressed on the surface of T-cells (column 1 lines 23-25 in particular) and that the increased prevalence of last state T cell activation antigen or VLA-1 in active juvenile chronic arthritis (column 1 line lines 56-57 in particular). Finally, the '966 patent teaches that VLA-1 molecule is involved in the binding of extracellular matrix materials (ECM) (column 8 lines 52-54 in particular).

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The claimed invention differs from the reference teachings only by the recitation of a function blocking antibody or fragment of said antibody, capable of binding an epitope of VLA-1 in claim 1.

Riikonen *et al* teaches that $\alpha 1 \beta 1$ integrin is also known as very late activation antigen-1 (VLA-1) and in vivo $\alpha 1 \beta 1$ integrin expression is seen in synovial lymphocytes of patients with rheumatoid arthritis (page 205 last paragraph in particular).

Fabbri *et al* teaches a functional monoclonal antibody (FB12) recognizing the human $\alpha 1$ integrin I-domain. Fabbri *et al* further teaches that FB12 mAB efficiently and specifically inhibits the binding of activated human lymphocytes to laminin, collagen type IV and fibronectin (see the entire document and page 48, left column 2nd paragraph in particular). Finally, Fabbri *et al* teaches that the $\alpha 1$ I domain has functional role in lymphocyte binding to ECM protein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the 1B3.1 monoclonal antibody taught by the '966 patent with functional monoclonal antibody FB12 as taught by Fabbri *et al* in a method of treating rheumatoid arthritis.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because FB12 monoclonal antibody has a functional role in lymphocyte binding to ECM protein as taught by Fabbri *et al* a critical molecule in synovial lymphocytes of patients with rheumatoid arthritis as taught by Riikonen *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

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9. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,788,966 (IDS Ref. No. AA), in view of Riikonen *et al* (Biochemical and Biophysical Research Communication 209:205-212, 1995).

The teachings of '966 patent have been discussed, *supra*. The '966 further teaches that members of a protein complex called very late antigens (VLA) are expressed on the surface of T-cells (column 1 lines 23-25 in particular) and that the increased prevalence of last state T cell activation antigen or VLA-1 in active juvenile chronic arthritis (column 1 line lines 56-57 in particular). Finally, the '966 patent teaches that VLA-1 molecule is involved in the binding of extracellular matrix materials (ECM) (column 8 lines 52-54 in particular).

The claimed invention differs from the reference teachings only by the recitation of a function blocking antibody or fragment of said antibody, capable of binding an epitope of VLA-1 in claim 1.

Riikonen *et al* teaches a functional monoclonal antibody (SR-84) recognizing the human $\alpha 1$ subunit which inhibit the adhesion of cells to matrix molecules. Riikonen *et al* further teaches that SR-84 mAB completely block the adhesion of Hela cells to type IV collagen (see the entire document and page 207 last paragraph in particular). Furthermore, Riikonen *et al* teaches that $\alpha 1\beta 1$ integrin is also known as very late activation antigen-1 (VLA-1) and in vivo $\alpha 1\beta 1$ integrin expression is seen in synovial lymphocytes of patients with rheumatoid arthritis (page 205 last paragraph in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the 1B3.1 monoclonal antibody taught by the '966 patent with functional monoclonal antibody SR-84 as taught by Riikonen *et al* in a method of treating rheumatoid arthritis.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because SR-84 monoclonal antibody inhibits the adhesion of VLA-1 with different collagenous components of extracellular matrix (ECM), and hence its important in $\alpha 1\beta 1$ integrin seen in synovial lymphocytes of patients with rheumatoid arthritis as taught by Riikonen *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.


10. No claim is allowed.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
February 10, 2003


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600